Original Research Article

Aplastic Anaemia: A review from a Tertiary Hospital in Nigeria.

ABSTRACT

Background: Aplastic anaemia is a relatively rare disease, characterized by the loss of haemopoietic stem cells in the bone marrow, exchanged with fat cells and pancytopenia in the peripheral circulation. The aim of this study was to evaluate the incidence , management and outcome of aplastic anaemia in children, over a four-year period, at the University of Port Harcourt Teaching Hospital, Nigeria.

Subjects and Methods: This was a retrospective study of case notes of all children with anaemia and bone marrow aspiration reports suggestive of aplastic anaemia in the Paediatric Haematology and Oncology Units of the Department of Paediatrics, University of Port Harcourt Teaching Hospital University Teaching Hospital, from January 1 st 2015 to December 31 st 2018. Information extracted for each patient included age, gender, diagnosis, haematologic parameters at diagnosis (White blood cell count, Haematocrit, Platelet count) and outcome. Data entry and analysis were done using the statistical package for social sciences (SPSS) version 22. Data analysis were done using descriptive statistics (proportions and frequencies) and presented in prose and frequency tables. Mean and standard deviations of quantitative data were obtained.

Results: A total of six children were diagnosed with aplastic anaemia over a four year period; giving an annual incidence of 0.0049 cases per year. The age range of the patients was between 3 to 11 years; (mean 8.2±3.7). The male female ratio was 2: 1. The mean (±SD) packed cell volume at diagnosis was 15± 3.2%, white cell count; 2.72± 0.76x 10^9/L, Absolute neutrophil count (ANC); 0.25± 0.17 x 10^9/L, and platelets; 17.33± 21.36 x 10^9/L. All 6(100%) of the patients presented with severe aplastic anaemia at diagnosis. Management of the patients included transfusion support with fresh unbanked whole blood, platelet concentrate , antibiotics, antifungal, antiviral and oral cyclosporine and intravenous methyl-prednisolone. All patients were blood transfusion dependent. The mean survival from diagnosis was 7.3± 3.08 months.

None of the patients had the benefit of bone marrow transplantation and anti-thymocyte immunoglobulin. Mortality rate was 83.3% and major cause of death was a combination of sepsis and thrombocytopaenic bleeding.

Conclusion: Aplastic anaemia is rare with short survival rate. There is need for the Federal Government to ensure the availability of bone marrow/stem cell transplantation centers across the country and make drugs such as cyclosporine and anti-thymocyte immunoglobulin affordable to ameliorate the condition .

KEY WORDS: APLASTIC ANAEMIA; CHILDREN; PORT HARCOURT; NIGERIA

INTRODUCTION

Aplastic anemia (AA) is a serious form of bone marrow failure which, if not treated, is associated with very high mortality. It is characterized by pancytopenia and hypocellular bone marrow and can result in serious clinical manifestations such as chronic anemia, hemorrhage, and infection[1] . It has also been linked to environmental or occupational toxins such as benzene, viral infection, contaminated water sources, and exposure to animal fertilizers and agricultural pesticides[2,3].

The incidence of AA in the Western countries is approximately 2 per million per year, but it occurs more commonly in the Far East, with a 2 to 3-fold higher[4]. The incidence varies according to geographical location. Following the introduction of immunosuppressive therapy (IST) with antithymocyte globulin (ATG), and allogeneic stem cell transplantation (SCT) in the 1980–90s, several studies have reported an improved outcome with a 5-year overall survival of approximately 70–80%[5].

The outcome of patients with severe aplastic anemia is influenced by patients' vari-ables such as severity of the disease , age, and choice of the initial treatment[6]. The mortality rate of severe aplastic anemia is high but treatment by allogeneic stem-cell trans-plantation or immunosuppression, has improved the prognosis in recent years, and greater than 75% of patients are now expected to have long- term survival with either therapy .This is not the case in Nigeria where bone marrow/stem cell transplantation and immunosuppressive drug therapy with antithymocyte globulin and cyclosporine are not readily accessible to Nigerians with aplastic anaemia. We therefore decided to evaluate the incidence , management and outcome of aplastic anaemia in children, over a four-year period, in our Hospital in Port Harcourt, Nigeria.

Subjects and Methods: This was a retrospective study of all children with anaemia and bone marrow aspiration reports suggestive of aplastic anaemia in the Paediatric Haematology and Oncology Units of the Department of Paediatrics, University of Port Harcourt Teaching Hospital(UPTH), Nigeria. The Case notes of all patients with established diagnosis of aplastic anaemia from January 1 st 2015 to December 31 st 2018 were reviewed. Ethical clearance was obtained from the Ethical Committee of the UPTH. Patients on cancer chemotherapy, radiation therapy and hypersplenism as well as lymphomas with bone marrow involvement were excluded from the study. Information extracted for each patient included age, gender, date of diagnosis, haematologic parameters at diagnosis (White blood cell count, Haematocrit, Platelet count) and outcome.

The severity of aplastic anemia was defined according to the widely accepted criteria described by Camitta et al[7]. Severe disease was defined as the presence in two of three blood counts of an absolute neutrophil count $<0.5\times10^9$/L, platelet count $<20\times10^9$/L, and reticulocytes <1%. Extreme neutropenia (absolute neutrophil count $<0.2\times10^9$/L) defined very severe aplastic anemia. All other cases were defined as moderate. Duration of survival is taken as the interval between the date of diagnosis and death or date patient was last seen on follow up.

Data entry and analysis was done using the statistical package for social sciences (SPSS) version 22. Data analysis were done using descriptive statistics (proportions and frequencies) and presented in prose and frequency tables. Mean and standard deviations of quantitative data were obtained.

RESULTS:

A total of six children were diagnosed with aplastic anaemia over a four year period; giving an annual incidence of 0.0049 cases per year. The age range of the patients was between 3 to 11 years; (mean 8.2±3.7). The male female ratio was 2: 1(Table1).

The haematological parameters of the subjects are as shown in Table 2: The mean (±SD) packed cell volume at diagnosis was 15± 3.2%, white cell count; 2.72± 0.76x 10^9/L, Absolute neutrophil count (ANC); 0.25± 0.17 x 10^9/L, and platelets; 17.33± 21.36 x 10^9/L.

Blood film reports of all the 6 cases reviewed uniformly showed normocytic, normochromic anaemia with leucopenia, neutropenia with predominant lymphocytes. Platelets were reduced but with normal morphology. There were no appreciable dysplasia.

Bone marrow aspirate of the 6 patients were markedly hypocellular. Erythrocytes and neutrophils were markedly reduced. Lymphocytes were the majority of the cells seen. Plasma cells were reduced and megakayopoeisis were severely decreased.

All the patients presented fever, paleness of the body and bleeding from the mouth and nose. The duration of the illness ranges from 2-6 weeks with diagnosis of severe aplastic anaemia at presentation. Management of the patients included transfusion support with fresh unbanked whole blood, platelet concentrate, , antibiotics, antifungal, antiviral and oral cyclosporine and intravenous methyl-prednisolone. All patients were blood transfusion dependent. The mean survival from diagnosis was 7.3± 3.08 months. The longest surviving patient was followed up for 1year. Late presentation was an important issue in the majority of cases seen.

None of the patients had the benefit of bone marrow transplantation and anti-thymocyte immunoglobulin. Mortality rate was 5(83.3%) and major cause of death was a combination of sepsis and thrombocytopaenic bleeding.

DISCUSSION:

The incidence of aplastic anaemia in this study was incidence of 0.0049 cases per year. Earlier epidemiological studies have shown a broad variation in incidence depending on time and geographical location [8]. Studies from Europe and the United States in the 1960–70s showed a very high incidence (six to ten cases of AA per million per year)[8]. In addition, in some studies, there was an association with toxic agricultural substances [8-10]. This was later confirmed by data from Spain published in 2008, with an overall incidence of 2.34 per million per year[11]. In some studies, the incidence has also been reported to be slightly higher among females[5,8], while data from Turkey and Bangkok have instead shown a male predominance[5,8], which agrees with our study. Krista et al in Sweden reported no differences between female and male incidence rate[8].

The age range of affected patients in this study shows that the school age population is largely affected with a mean age of 8.2±3.7years. In comparism to other recent studies, the mean survival of patients with aplastic anaemia in this series is low. This is most likely due to bleeding and sepsis as a result of markedly low platelet and absolute neutrophil counts at presentation. Futhermore, laboratory parameters at presentation showed severe aplastic anaemia at diagnosis. This could also be a contributory factor to the short survival.

Management of thrombocytopaenic bleeding presents a special challenge in the absence of adequate platelet support services as red cell transfusion does not help and may indeed aggravate the situation and provoke further bleeding.[11] This is because red cell diapedesis is heightened in thrombocytopaenic states and microvascular capillary bleeding is thus worsened. Expressively, the management of aplastic anaemia in this study is suboptimal as platelet concentrate was not readily available.

The mean survival from diagnosis was 7.3± 3.08 months. Current survival rates where optimal management facilities and therapeutic options are available are significantly higher with reports of 70-90% five year survival and 51% at fifteen years[2]. The non-availability of bone marrow/stem cell transplantation is a major contributory factor to the very short survival

recorded in this study. Arewa et al in a 1992 review documented non-availability of bone marrow transplant facility in Nigeria as an important factor contributing to the poor survival of aplastic anaemia patients in Nigeria[12]. Bone marrow transplantation is now considered as the definitive management modality for a number of haematologic disorders including aplastic anaemia[13], it is unfortunate that centre offering this treatment in a country with a population of over 150 million is scarce.

Immunosuppressive therapy is an important alternative to bone marrow/stem cell transplantation in the management of aplastic anaemia. Effective immunosuppressive drugs such as antithymocyte globulin was scarce and not affordable. Nonetheless, steroids such as prednisolone, known to be ineffective in achieving the expected effect, was used as adjunct in the management of the patients in the absence of the potent immunosuppressive drugs such methyl prednisolone. Also, there was scarce transfusion support service for the supply of the much needed blood component (red cell and platelet concentrates) required for transfusing the patients as necessary. Platelet concentrates were not readily available, necessitating the use of fresh whole blood in the management of severe thrombocytopenia.

Conclusion: Aplastic anaemia is rare with short survival rate. There is need for Federal Government to ensure the availability of bone marrow/stem cell transplantation centers across the country and make drugs such as cyclosporine and anti-thymocyte immunoglobulin affordable to ameliorate the condition .

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TABLE 1: Age and Gender Distribution of Children with Aplastic Anaemia

Age(years)	Male	Female	Total
0-<5	0	1	1
5-<10	0	1	1
10-<15	1	3	4
Total	1	5	6

TABLE 2: Haematological Parameters of Children with Aplastic Anaemia at Presentation

Patients	PCV	WBC(x10^9/l)	Neutrophil(%)	Lymphocyte(%)	ANC(x10^3/l)	Platelet(x10^9/l)	Ret(%)
1	14	3.76	17.5	78.3	0.02	3	1.93
2	18	3.20	22	72.9	0.47	16	1.02
3	12	3.1	6.2	88.9	0.16	11	0.11
4	17	2.12	5	94	0.15	7	0.14
5	19	2.6	9	88	0.38	60	0.08
6	10	1.7	16	84	0.32	7	0.17
Mean	15±3.27	2.72± 0.76	12.6± 6.86	84.35± 7.14	0.25± 0.17	17.33± 19.50	0.58± 0.75

TABLE 3: Duration of Survival of the Patients with Aplastic Anaemia

Patients	Duration of Survival(in months)
1	4
2	10
3	6
4	5
5	7
6	12
Mean	7.3± 3.08